

## EMERGENCY CASEBOOK

## Co-trimoxazole induced acute thrombocytopenic purpura

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*Emerg Med J* 2003;20:e3(<http://www.emjonline.com/cgi/content/full/20/3/e3>)

A 58 year old man presented to the emergency department with rhinorrhagia, haematuria, and generalised petechiae and ecchymoses (fig 1). Two weeks before his admission, a 10 day course of co-trimoxazole double strength tablets (trimethoprim 160 mg and sulfamethoxazole 800 mg) twice daily was prescribed as treatment for a urinary tract infection caused by *E coli*. He stopped taking the drugs on his physician's advice two days before completion of treatment after he noticed easy bruising. The subsequent development of extensive purpuric lesions and rhinorrhagia brought him to the hospital. His medical history was notable only for moderate prostatic enlargement. On admission, his spleen was not palpable. A peripheral blood sample revealed a very low platelet count ( $<5 \times 10^9/l$ ) and a normal white blood cell count, leucocyte differential cell count, and haemoglobin level. The fibrinogen concentration, prothrombin time, partial thromboplastin time, and results of the patient's biochemistry tests were also normal. A search for antinuclear antibodies and anti-HIV antibodies was negative. Serological tests for Epstein-Bar virus, cytomegalovirus, mycoplasma, and toxoplasma were also negative. A bone marrow study revealed plentiful megakaryocytes of increased size. The co-trimoxazole treatment was considered the probable cause of the syndrome and the patient was given oral prednisolone treatment at a dose of 1 mg/kg daily. The thrombocytopenia and the accompanying clinical manifestations resolved in the next two weeks and the patient was discharged with a tapering four week course of oral prednisolone and has remained well since.

The use of certain drugs can induce thrombocytopenia by suppressing the production of platelets or by increasing the consumption of peripheral platelets by an immune mediated mechanism. In the case described here, the normal bone marrow excludes a myelosuppressive aetiology. Thrombocytopenia is an uncommon but serious side effect of the antimicrobial combination of trimethoprim and sulfamethoxazole.<sup>1,2</sup> Thirty one cases in seven years, including two deaths, have been reported to the Australian Drug Reactions Registry.<sup>1</sup> Female patients were affected twice as frequently as male patients. In 70% of the patients platelets counts were  $20 \times 10^9/l$  or less. Thrombocytopenia that is associated with this drug may occur at any age. Interference with folate metabolism has been postulated.<sup>2</sup> The drug has also been postulated to induce an autoantibody by acting as a hapten and there have been reports in which the serum has been shown to contain an anti-platelet autoantibody requiring sulfamethoxazole or co-trimoxazole for activity.<sup>2</sup>

With drug induced immune thrombocytopenia, bleeding usually appears abruptly and may be of life threatening severity. Severe thrombocytopenia usually develops within hours in sensitised patients ingesting the drug<sup>3</sup>; however, a minimum of six to seven days are required to start a primary immune response in people taking the drug for the first time. Some patients receiving long term treatment with a drug do not develop thrombocytopenia for months or years, a characteristic that seems more dependent on the host than the type of the drug. Recovery can usually be expected upon withdrawal of the drug. In severe and symptomatic drug induced immune thrombocytopenia, treatment with systemic corticosteroids or



**Figure 1** Diffuse petechiae in the legs of the patient.

high dose intravenous immunoglobulin may be effective in correcting the thrombocytopenia.<sup>3</sup> Emergency treatment for life threatening bleeding consists of platelet transfusion, high doses of corticosteroids (for example, 1 g methylprednisolone) given intravenously and intravenous immunoglobulin (1 g/kg daily for two days). Co-trimoxazole is often recommended as first line treatment for urinary tract infections, bronchitis, sinusitis, and as a prophylaxis and treatment for *Pneumocystis carinii* pneumonia. Practitioners should be aware of this rare adverse effect of co-trimoxazole and closely observe patients for cutaneous manifestations and bleeding attributable to thrombocytopenia in order to withdraw the drug promptly.

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Accepted for publication 27 November 2002

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